Remarks

Claims 12-15, 17-22, and 26-33 are currently pending in this application.

Applicants respectfully request that the amendments be entered into the specification. The amendments to the specification are of an editorial nature to place the plant names in italic form and to correct minor deficiencies noted by the Examiner.

In addition, at page 9, line 16, the term "1.98 g of hexane" has been amended to read "1.9 Kg of hexane". It would be clear to one skilled in the art that this was an obvious mistake since 1.98 grams of hexane could not defat 0.3 kilograms of *Argania spinosa* cake.

Applicants have not changed the nomenclature in regard to arganin A-J. Applicants submit that this is the proper nomenclature and the Examiner's suggestion that the term be amended to "arginine" A-J is not proper nomenclature in this art. The arganins A-J are compounds of the formula (1) shown at page 4, lines 13-14. As is well known in the art, arginine is an amino acid of the formula $C_6H_{14}O_2N_4$ which is found in animal and vegetable proteins. However, the saponin shown in formula (1) at page 4 does not contain any nitrogen and is obviously not an amino acid. Applicants therefore respectfully submit that arginine is not the same or equivalent to the arganin A-J useful in the practice of the present invention. Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

The claims have been amended to indicate that the extract of the plant *Argania spinosa* contains at least one of proteins and saponins. The amendments to the claims clearly distinguish the present invention from the teachings of Hatinguais et al. (FR2553788A1). The amendment to the claims which require that the extract contain at least one of saponins and proteins clearly distinguish over the teaching of Hatinguais et al. As the Examiner states, Hatinguais et al. is directed to preparation of a stable liquid extract of argan fruit in an apolar solvent. The purified stable liquid extract of

Hatinguais et al. does not contain at least one of saponins and proteins. Applicants therefore respectfully submit that Hatinguais et al. does not make obvious any of the claims presently in the application, and especially claim 32.

Applicants respectfully request that the requirement for restriction be reconsidered and withdrawn. As shown above, Hatinguais et al. does not destroy the unity of the invention of the claims presently in the application. All of the claims presently in the application require that the extract contain proteins and saponins which are not present in the purified stable liquid lipid extract of Hatinguais et al. Since Hatinguais et al. does not destroy the unity of invention, Applicants respectfully request that the requirement for restriction be reconsidered and withdrawn.

The unity of invention of the present application is based on the discovery of the anti-5-α-reductase activity of the extract of the invention containing the at least one of proteins and saponins. The particular proteins and saponins and the mixture of the proteins and the various saponins provided by the plant *Argania spinosa* provides a reduction in the activity of 5-α-reductase which is a fundamental cause of the various conditions treated by the method of the present invention. Hatinguais et al. neither teaches nor suggests utilizing a composition containing at least one of proteins and saponins of the plant *Argania spinosa* and this is the technical feature on which the unity of invention is based, Applicants respectfully submit that the requirement for restriction is improper and respectfully request that it be reconsidered and withdrawn.

The use of the trademark SkinEthic has been noted as a reconstructed epidermis.

Applicants have not adopted the Examiner's suggestion for a new title. Applicants submit that the title as amended clearly points out the present invention.

The Examiner has objected to the claims because the term "*Argania spinosa*" was not in italics. The claims as amended and the specification as amended utilize the term "*Argania spinosa*" in italics. Applicants submit that this amendment should

overcome the Examiner's objections.

The Examiner has objected to claims 27 and 28 because the use of the term "Arganin A", "Arganin B", etc. As discussed above, Applicants submit that the term arganin in reference to A-J are the correct nomenclature which refers to the various saponins found in parts of the *Argania spinosa* plant and especially in the seeds.

Claims 14, 15, 24, 25, 27, 28, 30, and 31 stand rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method for reducing the activity of 5-α-reductase. Applicants respectfully request that the rejection be reconsidered and withdrawn.

The specification discloses a preparation of an extract of *Argania spinosa* from the defatted seeds of the plant. The extract was obtained utilizing aqueous ethanol extractant and done at room temperature. The extract was tested by an *in vitro* method for determining the reduction in the activity of 5-α-reductase. Since this is the common technical feature which connects all of the claims in the application and the discovery that the extract of *Argania spinosa* which contains at least one of proteins and saponins, reduces the activity of 5-α-reductase, Applicants respectfully submit that they have shown the activity of the extract of the present invention for the effects cited. In addition, the tests indicated that the extract penetrates the epidermis and is not toxic to keratinocytes. Applicants submit that the showing of the reduction in 5-α-reductase activity and penetration of the epidermis, which is a required action for the methods of all of the claims in the application, is sufficient to teach one skilled in the art how to utilize the present invention.

In addition, beginning at page 5 and extending through page 8, line 18, the specification teaches additional methods for preparing the extract of *Argania spinosa* containing at least one of proteins and saponins.

One skilled in the art having before him the present application, would have no difficultly in preparing the extract of *Argania spinosa* without any additional

experimentation. The testing of the extract could be readily accomplished by application of the extract preferably in a formulation adapted for cosmetic or dermatological application, without any additional experimentation. The specification discloses the various amounts of the extract which should be in the composition and the preferable amounts of proteins and saponins. Applicants respectfully submit that one skilled in the art would not have any difficulty in preparing the extract of *Argania spinosa* and preparing a cosmetic or dermatological composition and testing the composition as set forth in the present application.

Applicants respectfully submit that the application is directed to one skilled in the art. Applicants submit that one skilled in the art would have no difficulty preparing the extract of *Argania spinosa*, preparing a cosmetic or dermatological preparation containing the extract and applying the cosmetic or dermatological composition to the skin and observing the effect on seborrhea, acne, and unwanted hair growth. When these effects were noted, one skilled in the art from reading this specification would understand that the effects were due to a reduction in the activity of 5-α-reductase. Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 112, first paragraph.

The claims also stand rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is non-enabling. Applicants respectfully submit that the specification is enabling for the methods set forth. As stated above, the effects which are treated by the methods, are all the result of 5-α-reductase activity. As shown in the examples, the present invention clearly reduces the activity of 5-α-reductase. One skilled in the art wishing to determine whether the composition of the invention was effective for treating seborrhea, acne, and unwanted hair growth would merely have to prepare an extract as shown in the examples or in the discussion of the extracts proteins and saponins in the specification, and applying the extract to the area of the skin which is to be treated, alone or in a cosmetic or dermatological composition, and

observing whether the effect is achieved. Applicants do not believe that there is a simpler method for carrying out the methods of the invention.

One skilled in the art observing the reduction in the seborrhea, acne, or unwanted hair growth would be directed to the reduction in the activity of 5-α-reductase by the effects noted.

Since as shown in the examples, the extract is not toxic to certain skin cells, one skilled in the art would apply the extract in the preferred ranges to the area to be treated. Applicants respectfully submit that the specification clearly supports the breadth of the claims and one skilled in the art would have no difficulty in preparing the extract, applying the extract to the skin and observing the effects. Applicants respectfully submit that there would be no undue experimentation by one skilled in the art in carrying out the invention. In fact, there would be no need for any experimentation since one skilled in the art could carry out the invention by simply preparing the extract and applying the extract directly to the skin and observing the effects. Applicants do not know any simpler and experimentation-free testing which would be required to practice the present invention.

Applicants respectfully submit that the present invention is simple in that the specification completely discloses many methods for preparing the extract and discloses that the extract can be prepared utilizing the components known for cosmetic and dermatological compositions. The preferred amounts of the extract in the composition are set forth at page 9, lines 5-10 and could be readily prepared by one skilled in the art. If by the non-enabling disclosure the Examiner means that Applicants have not enabled one skilled in the art to prepare and apply the absolutely most effective composition, the Examiner is probably correct. Applicants have not carried out a PhD thesis study to determine the absolutely best method and particular concentrations for preparing the extract and the cosmetic and dermatological compositions. However, Applicants have provided guidelines in relation to methods for

forming the extract and the preferred amounts of the extract which should be in the compositions applied to the skin. Applicants have presented the best modes and methods for extraction and concentration of which they are aware. However, many of the additional methods of forming the extract and the concentrations of the extract in the cosmetic or dermatological compositions are suitable for achieving the effects set forth in the claims. Applicants do not consider that there would be a major amount of experimental testing required to carry out the invention. As a starting point, since Applicants have pointed out that the extracts are not toxic to skin cells, one skilled in the art could prepare an extract and provide the maximum amounts of the extract set forth in the specification in a dermatological or cosmetic formulation, apply the composition to the skin and observe the effects obtained. Applicants submit that this would not require undue experimentation and one skilled in the art could rapidly determine the effectiveness of the composition. Applicants therefore respectfully submit that the claims are fully supported in the specification.

Applicants respectfully submit that it is not necessary to provide examples of each and every composition which may fall within the broad ranges of the compositions set forth in the specification and the claims. Applicants submit that in a method claim, it is not always necessary to provide an example of each and every embodiment. Looking at the specification as a whole, Applicants have provided information for preparing an extract, have provided preferred compositions of the extract and preferred compositions containing particular amounts of the extract. Applicants submit that this is ample support for the claims in the present application.

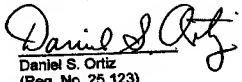
The amendment to claim 14 overcomes the rejections of claims 14 and 15 on the grounds of indefiniteness. The amendments to claim 14 and 15 clearly overcome the indefinite rejections set forth by the Examiner.

In view of the above discussion, and the fact that Hatinguais et al. neither teaches nor suggests the present invention, Applicants respectfully request that the

requirement for restriction be reconsidered and withdrawn.

Favorable consideration of the claims in their amended form is respectfully requested.

Respectfully submitted,



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Enc.: 1. Marked-Up Specification
2. Substitute Specification
3. Request for Extension of Time

MARKED-UP SPECIFICATION

PATENT
CASE NO.: C 2766 PCT/US

~~Use of an Extract from the Plant Argania Spinosa~~

USE OF COSMETIC AND DERMATOLOGICAL PREPARATIONS CONTAINING AN EXTRACT FROM THE PLANT *ARGANIA SPINOSA*

Field of the Invention

This invention relates generally to cosmetic and/or dermopharmaceutical care products and, more particularly, to the use of extracts of the plant ~~Argania spinosa~~ *Argania spinosa* for the production of anti-acne and/or anti-seborrhoea preparations and preparations with anti-5-α-reductase activity.

Prior Art

Greasy and acne-affected skin shows increased secretion of sebum and tallow through over-activity of the sebaceous glands. The triglycerides present in the secretions of the sebaceous glands are decomposed on the skin by lipases of various microorganisms such as, for example, Corynebacterium acnes, Staphylococcus epidermis and Pytirosporum ovale and free fatty acids are released. Some of these free fatty acids lead to the characteristic inflammatory phenomena of the acute stage of acne.

The conversion of testosterone into 5-dihydrotestosterone (5-DHT) by the enzyme 5-α-reductase has been found to be one of the causes of increased sebaceous gland secretion. Accordingly, the activity of the enzyme 5-α-reductase, which can be found in particular in the sebaceous glands and in apocrine glands and in keratinocytes and fibroblasts, is of particular importance to skin affected by acne or seborrhoea.

Today, cosmetic preparations are available to the consumer in a variety of combinations. Nevertheless, there is a need on the market for products with an improved performance spectrum. In this connection, consumers demand dermatological compatibility and the use of natural

products. In addition, it is desirable to obtain distinctly better products by combining already known active principles or by discovering new applications for already known classes of substances. More particularly, extracts of plants and their ingredients are being more commonly used in cosmetic and pharmaceutical products. However, there are many plants and their potential effects which have yet to be discovered and many new applications of already known classes of substances are time and again causing surprise.

It has been known for some time that many saponins obtained from various plants and microorganisms show anti-radical, analgesic and also anti-inflammatory activity. Such activity was also demonstrated for the saponins isolated from ~~Argania spinosa~~ *Argania spinosa* by Alaoui et al. [Alaoui K. et al.; **Annales pharmaceutique francaices, 1998, 56, 220-228**]. In addition, some saponins have been found to show antibiotic and fungistatic activity. Saponins and especially the triterpene saponins are made up of a tetra- or pentacyclic triterpene aglycon and one or two glycosidically linked sugar chains.

The problem addressed by the present invention was to find new applications for highly compatible extracts of renewable vegetable raw materials rich in active components, more particularly active components for the treatment of acne-affected and seborrhoeic skin.

Description of the Invention

The present invention relates to the use of extracts of the plant ~~Argania spinosa~~ *Argania spinosa* (L.) Skeels, hereinafter referred to in short as ~~Argania spinosa~~ *Argania spinosa*, for the production of anti-acne preparations, for the production of anti-seborrhoea preparations and for the production of preparations with anti-5-α-reductase activity.

It has surprisingly been found that preparations with an excellent effect in anti-acne preparations and in anti-seborrhoea preparations,

coupled with high dermatological compatibility, can be produced by using extracts of the plant ~~Argania spinosa~~ *Argania spinosa*. Accordingly, they may be used with outstanding effect against greasy skin, acne skin and greasy scalps, even in people with sensitive skin. The preparations produced show distinct anti-5-α-reductase activity. Accordingly, a particular embodiment of the present invention is the use of extracts of the plant ~~Argania spinosa~~ *Argania spinosa* for the production of preparations for treating unwanted hair growth in women, more particularly unwanted hair growth occurring after the menopause. This unwanted hair growth occurs in particular on the face, above all around the mouth, or on the legs. Unwanted excessive hair growth in women, particularly after the menopause, is associated with hyperactivity of 5-α-reductase. The unwanted, often excessive hair growth on certain parts of the face or on the legs can thus be effectively inhibited by using extracts of the plant ~~Argania spinosa~~ *Argania spinosa*.

~~Argania spinosa~~ *Argania spinosa*

The extracts used in accordance with the invention are obtained from plants of the family ~~Sapotacea~~ *Sapotaceae*, more especially from ~~Argania spinosa~~ *Argania spinosa* (L.) Skeels, hereinafter referred to simply as ~~Argania spinosa~~ *Argania spinosa*. This plant is a tree which is mainly found in Morocco on the western side of the Atlas mountains. On its gnarled trunks and thorny branches, it forms berries the size and shape of olives with one or two seed kernels. The nutty-tasting oil from the seed kernels is used inter alia as an edible oil.

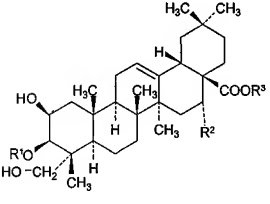
In the context of the present invention, the term plant is intended to encompass both whole plants and plant parts (leaves, roots, stem, bark, flowers, fruits, fruit flesh and seed kernels) and mixtures thereof. According to the invention, the seed kernels of the fruit of the plant, more particularly the extraction of the residue from defatted seed kernels, are particularly

preferred for the extraction of the saponins.

Saponins

Saponins in the context of the present invention are, basically, any saponins which can be isolated from the plant ~~Argania spinosa~~ *Argania spinosa*.

Saponins differing in structure from saponins from other plants are obtained from the residue accumulating in the extraction of oil from the seed kernels of ~~Argania spinosa~~ *Argania spinosa* [Charrouf Z., et al.; **Phytochemistry, 1992, 31; 2079-2086**]. The saponins in question are known as arganin A, arganin B, arganin C, arganin D, arganin E, arganin F and ~~misaponin~~ mi-saponin A. The useful saponins arganin G, arganin H and arganin J can be isolated from the stem of the plant [Oulad-Ali A., et al.; **J. Nat. Prod.; 1996, 59, 193-195**]. The aglycon of these saponins has the structure (I) shown below. The saponins mentioned differ in the sugar units at R1 and R3 and in a hydroxy group at R2. R3 is a tetrasaccharide while R1 is a mono- or disaccharide (for example 1,6-diglucose for arganin A and B).



The saponins according to the invention show low toxicity in toxicological tests on mice and rats. In tests on human fibroblasts, the

inventors were also able to demonstrate far lower toxicity by comparison with other saponins, for example from ~~Gypsophila paniculata~~ *Gypsophila paniculata*.

The saponins to be used in accordance with the invention correspond to arganin A, arganin B, arganin C, arganin D, arganin E, arganin F, ~~misaponin~~ mi-saponin A and to arganin G, arganin H and arganin J. They may be used as a mixture of two or more or in pure form in cosmetic and/or pharmaceutical preparations. Mixtures of arganin A, arganin B, arganin C, arganin D, arganin E, arganin F, ~~misaponin~~ mi-saponin A - the percentages of the saponins in the mixtures being variable – are particularly preferred. Extracts containing a high percentage of arganin A are preferably used. The use in accordance with the invention of extracts containing at least 6% by weight, preferably 8% by weight and more particularly at least 10% by weight arganin A, based on the dry weight of the extract, is distinguished by particularly pronounced effects.

Proteins

Proteins in the context of the invention are understood to be proteins which can be isolated from the plant ~~Argania spinosa~~ *Argania spinosa*. It is preferred to extract the seed kernels, more particularly the defatted seed kernels after extraction of the oil. Accordingly, preparations containing native proteins obtained from an extract of the seed kernels, more particularly the defatted seed kernels of ~~Argania spinosa~~ *Argania spinosa*, represent a particular embodiment of the invention.

In the context of the invention, the preferred extraction of the defatted seed kernels is understood to mean that the residue – a kind of cake – from the extraction of oil from the seed kernels of ~~Argania spinosa~~ *Argania spinosa* is preferably extracted. This oil extraction residue which is preferably extracted contains 3 to 10% by weight of residual oil. The proteins according to the invention in this residue are completely separated

from the residual oil. Besides proteins, other substances occurring naturally in ~~Argania spinosa~~ *Argania spinosa* plants, which can be extracted under the same conditions, can be co-extracted.

In another embodiment of the invention, the preparations according to the invention contain native proteins which are obtained by extraction with water at a pH of or below 12, preferably between 3.5 and 6.5 and more particularly between 5.5 and 6.5 or between 3.5 and 5.5 and, optionally, subsequent drying, for example spray or freeze drying. The pH range selected is dependent upon the protein fraction to be isolated.

The native proteins which can be extracted from the plant ~~Argania spinosa~~ *Argania spinosa*, more particularly from the seed kernels of the plant, may have molecular weights in the range from 10,000 Da to more than 500,000 Da. They may advantageously be divided into the following groups of molecular weight ranges. Native proteins with a molecular weight above 500,000 Da, native proteins with a molecular weight in the range from 170,000 to 250,000 Da and native proteins with a molecular weight in the range from 10,000 to 18,000 Da can be extracted.

Accordingly, other embodiments of the present invention are, on the one hand, preparations containing native proteins with a molecular weight above 500,000 Da, preparations containing native proteins with a molecular weight in the range from 170,000 Da to 250,000 Da and preferably in the range from 170,000 Da to 210,000 Da and preparations containing native proteins with a molecular weight in the range from 10,000 to 18,000 and preferably in the range from 13,000 to 16,000.

The percentage content of proteins in the extract used in accordance with the invention should preferably be at least 3% by weight, preferably at least 4% by weight and more particularly at least 5% by weight, based on the dry weight of the extract.

Extraction

The extracts to be used in accordance with the invention may be prepared by known methods of extracting plants or parts thereof. Particulars of suitable conventional extraction processes, such as maceration, remaceration, digestion, agitation maceration, vortex extraction, ultrasonic extraction, countercurrent extraction, percolation, repercolation, evacolation (extraction under reduced pressure), diacolation and solid/liquid extraction under continuous reflux in a Soxhlet extractor, which are familiar to the expert and which may all be used in principle, can be found, for example, in **Hagers Handbuch der pharmazeutischen Praxis (5th Edition, Vol. 2, pp. 1026-1030, Springer Verlag, Berlin-Heidelberg-New York 1991).** Fresh or dried plants or parts thereof are suitable as the starting material although plants and/or plant parts which may be mechanically size-reduced before extraction are normally used. Any size reduction methods known to the expert, for example crushing with a mortar, may be used. In one particular embodiment, the extracts used are obtained by extraction of the stem, roots, leaves, flowers or fruits. Extraction of the seed kernels is particularly preferred.

Preferred solvents for the extraction process are organic solvents, water or mixtures of organic solvents and water, more particularly low molecular weight alcohols, esters, ethers, ketones or halogenated hydrocarbons with more or less large water contents (distilled or non-distilled), preferably aqueous alcoholic solutions with a temperature above 20° (hereinafter referred to as room temperature). Extraction with water, methanol, ethanol, acetone, propylene glycols, polyethylene glycols, ethyl acetate, dichloromethane, trichloromethane and mixtures thereof is particularly preferred. The extraction process is generally carried out at 20 to 100°C and preferably at 80 to 85°C, more particularly at room temperature. In one possible embodiment, the extraction process is carried out in an inert gas atmosphere to avoid oxidation of the ingredients of the extract. The extraction times are selected by the expert in dependence

upon the starting material, the extraction process, the extraction temperature and the ratio of solvent to raw material, etc. After the extraction process, the crude extracts obtained may optionally be subjected to other typical steps, such as for example purification, concentration and/or decoloration. If desired, the extracts thus prepared may be subjected, for example, to the selective removal of individual unwanted ingredients. The extraction process may be carried out to any degree, but is usually continued to exhaustion. Typical yields (= extract dry matter, based on the quantity of raw material used) in the extraction of dried plants or dried plant parts (optionally defatted) are in the range from 3 to 20 and more particularly 4 to 16% by weight. The present invention includes the observation that the extraction conditions and the yields of the final extracts may be selected according to the desired application. If desired, the extracts may then be subjected, for example, to spray drying or freeze drying.

According to the invention, the extracts of this plant contain 10 to 99% by weight of saponins, preferably 15 to 70% by weight. The quantity in which the plant extracts are used in the anti-acne preparations, in the anti-seborrhoea preparations and in preparations with anti-5-α-reductase activity is determined by the concentration of the individual ingredients. The total quantity of plant extract present in the preparations is generally 0.01 to 25% by weight, preferably 0.03 to 5% by weight and more particularly 0.03 to 0.4% by weight, based on the final preparation.

The plant extracts used preferably contain proteins and saponins in the described quantity ranges in combination.

Commercial Applications

Cosmetic and/or pharmaceutical preparations

The use of extracts from the plant ~~Argania spinosa~~ *Argania spinosa* for the production of anti-acne preparations, anti-seborrhoea preparations

and preparations with anti-5-α-reductase activity results in cosmetic and/or pharmaceutical preparations such as, for example, creams, gels, lotions, alcohol and water/alcohol solutions, emulsions, hair shampoos, hair lotions, foam baths, shower baths, wax/fat compounds, stick preparations, powders or ointments. These preparations may additionally contain mild surfactants, oil components, emulsifiers, pearlizing waxes, consistency factors, thickeners, superfatting agents, stabilizers, polymers, silicone compounds, fats, waxes, lecithins, phospholipids, biogenic agents, UV protection factors, antioxidants, film formers, swelling agents, hydrotropes, solubilizers, preservatives, perfume oils, dyes and the like as further auxiliaries and additives.

The total percentage content of auxiliaries and additives may be from 1 to 70% by weight, preferably from 20 to 50% by weight and more particularly from 5 to 40% by weight, based on the final preparation of the cosmetic and/or pharmaceutical preparations. The preparations may be produced by standard hot or cold processes and are preferably produced by the phase inversion temperature method.

Examples

Example 1: preparation of the saponin crude extract

0.3 kg of an ~~Argania spinosa~~ *Argania spinosa* cake (from the seeds after extraction of the oil) were defatted with 1.98 [[g]] Kg of hexane (1 hour at 80°C). The defatted cake was then dried for 24 hours at room temperature. 0.12 kg of the defatted and dried cake were made up with 2 liters of 80% by vol. ethanol in a stirred vessel. The mixture was stirred for 16 hours at room temperature. The solids were then removed by filtration. The filtered solution forms the crude extract from which ethanol was removed by evaporation. Finally, the residue was freeze-dried.

Principle of the test

Reconstructed epidermis – ~~comparably~~ comparable to living skin – contains the entire enzymatic mechanism required for the metabolization of testosterone. The test with reconstructed epidermis in vitro is more appropriate because the 5-α-reductase remains in a biological system which comes very close to the in vivo system and which cannot be created by purified enzymes. This test is also relevant because the keratinocytes at the differentiation stage come closer to the in vivo test than when keratinocytes are used in monolayers [Bernard F.-X. et al., 2000, **Int. J. Cosmetic Science, 22, 397-407, Expression of type 5-alpha-reductase and metabolism of testosterone in reconstructed human epidermis – SkinEthic: a new model for screening skin targeted androgen modulators**].

Test setup:

Material:

Epidermis SkinEthic® (a reconstructed epidermis) (17 days, 0.63 cm^2) in culture, 37°C, 5% CO_2

Reference substance: Finasteride

Testosterone: [4—14-C] Testosterone (Amersham, CFA129, 56 mCi/mmole), 250 nCi/epidermis

~~Argania~~ *Argania spinosa* saponin extract of Example 1

Treatment:

The epidermis was precultivated for 24 hours on plates with 24 positions. The experiments with the products and the reference substance Finasterid (10 µm) were carried out three times (3 epidermises per experiment). After treatment for 24 hours, the media of the subepidermis were renewed and replaced by 300 µl of fresh culture medium. 100 µl of radioactively marked testosterone solution were applied to the upper

surface (horny layer) of the epidermis ~~(TO)~~ (to). After another 24 hours, the subepidermis medium was removed for analysis.

The viability of the keratinocytes in the various epidermis samples was determined by the MTT method at the end of the test.

Extraction and analysis:

In order to determine the transepidermal diffusion, quantities of 20 µl of each culture medium were removed and counted in a liquid scintillation counter.

The steroids present in the culture medium were extracted for analysis of the metabolism and separated into their molecular derivatives by thin-layer chromatography (on silica gel). The quantity of transformed testosterone was determined by radioactive counting of the various spots using a phosphoimager.

Results:

The survivability of the treated epidermis and the transepidermal diffusion are shown in Table 1.

Table 1

Diffusion of ^{14}C testosterone (and metabolites) by reconstructed human epidermis (SkinEthic®) and survivability of the tissue at the end of the test (t=24 hours)

Treatment	% ^{14}C Testosterone	Nmole steroid	Survival rate in %
Total testosterone	/	4,5	/
Control	100	2.2	100
Finasterid 10 µm	110	2.4	101
~~Argania~~ *Argania* extract of Example 1			
0.003%	98	2.2	98
0.001%	100	2.2	101

The survivability of untreated epidermis (control) and Finasterid-

treated epidermis was identical with that of the extract-treated samples (2 concentrations).

For the transepidermal diffusion, approximately an average of the initial radioactivity was detected in the culture medium after incubation for 24 hours. The treatment with Finasterid resulted in a slight increase in the diffusion of steroids through the reconstructed epidermis (110% of the control).

However, the analyzed extract did not influence the diffusion of steroids through the epidermis (value between 98 and 100% of the control).

The metabolization of testosterone is summarized in Table 2.

Table 2

Influence of the treatment with ~~argania~~ *Argania* extract on the production of 5-DHT. Analysis by phosphoimager in connection with the accumulated radioactivity

Treatment	5-DHT formed in %
Control	100
Finasterid 10 µM	8
~~Argania~~ *Argania* saponin extract of Example 1	
0.001%	61%
0.003%	74%

The analyzed extract shows a distinct reduction in the production of 5-DHT – 39 and 26% inhibition. In a concentration of only 0.001% by weight, there is already evidence of a significant inhibition of the 5-α-reductase activity without toxic effects influencing the survivability of the cells (determined by the MTT test).

CLAIMS

1. The use of extracts of the plant Argania spinosa for the production of anti-acne preparations.

2. The use of extracts of the plant Argania spinosa for the production of anti-seborrhoea preparations.

3. The use of extracts of the plant Argania spinosa for the production of preparations with anti-5-α-reductase activity.

4. The use of extracts of the plant Argania spinosa as claimed in claim 3 for the production of preparations with anti-5-α-reductase activity for the treatment of unwanted hair growth in women, more particularly for the treatment of unwanted hair growth occurring after the menopause.

5. The use claimed in at least one of claims 1 to 4, characterized in that the extracts contain proteins and/or saponins.

6. The use claimed in any of claims 1 to 5, characterized in that the extracts contain saponins selected from the group consisting of arganin A, arganin B, arganin C, arganin D, arganin E, arganin F, arganin G, arganin H, arganin J and misaponin A.

7. The use claimed in at least one of claims 1 to 6, characterized in that the extracts contain arganin A in quantities of at least 6% by weight, based on the dry weight of the extract, as the saponin.

8. The use claimed in at least one of claims 1 to 7, characterized in that the extracts contain at least 3% by weight of proteins, based on the dry weight of the extract.

9. The use claimed in at least one of claims 1 to 8, characterized in that the extracts are used in quantities of 0.01 to 25% by weight, expressed as dry weight and based on the preparation.

10. The use claimed in at least one of claims 1 to 9, characterized in that the extract is obtained by extraction of plant parts selected from the group consisting of the leaves, the stem, the bark, the flowers, the fruits, the fruit flesh and the seed kernels.

11. The use claimed in at least one of claims 1 to 10, characterized in that the extract is obtained by extraction of the seed kernels and/or the defatted seed kernels from the fruit of the plant.